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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/630,319	07/31/2000	Arthur M. Krieg	C1039 7042	5464

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	9

DATE MAILED: 03/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/630,319	Applicant(s) KRIEG ET AL.	
	Examiner Jane Zara	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 42-131* is/are pending in the application.

4a) Of the above claim(s) *1,42-87,102 and 105-131* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *88-101,103 and 104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 July 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: *attachment*.

DETAILED ACTION

Claims 1, 42-131 are pending in the instant application.

Specification

Figures 4B, 5, 6, 7, 8A, 8B and 9-15 are missing from the specification.

Election/Restriction

Claims 1, 42-87, 102 and 105-131 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Applicant's election with traverse of Group V in Paper No. 8 is acknowledged. The traversal is on the ground(s) that a search and examination of all of the presented claims would not require an undue burden. This is not found persuasive because the searches required for properly examining all of the claims would not be coextensive, and would require considerations and searches of different and distinct databases, art and issues..

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

Claim 104 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what is meant by the CpG oligonucleotide being "stabilized" (i.e. Is the oligonucleotide stabilized from nuclease degradation by incorporating modifications such as phosphorothioate internucleotide linkages..?). Clarification is requested.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 88-101, 103 and 104 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for stimulating various immune associated responses, comprising B cell and monocyte activation, and producing the conversion from a Th2 to a Th1 type immune response in an organism, comprising the administration of an unmethylated CpG containing oligonucleotide, does not reasonably provide enablement for the treatment and prevention of any and/or all bacterial infections in an organism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to the prevention and treatment of any bacterial infection in an organism comprising the administration of CpG containing oligonucleotides.

The following factors have been considered in determining that the specification does not enable the skilled artisan to make and/or use the invention over the scope claimed.

rather for lack of enablement for the methods claimed.

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. Applicants have not provided guidance in the specification toward a method of preventing and/or treating any and/or all bacterial infections in an organism comprising the administration of CpG containing oligonucleotides. The specification teaches the induction of B cells in human spleen cells in vitro following the administration of unmethylated CpG containing oligonucleotides, as well as the conversion from a Th2 to a Th1 immune response in purified human B cells in vitro (i.e. as determined by an increase in IL-12 secretion, an increase in natural killer cell activation following increased IL-12 secretion, and an increase in interferon-gamma secretion by natural killer cells). The specification also teaches a shift from a Th2 to a Th1 immune response (as indicated by an increase in IL12 secretion and an increase in interferon-gamma production) in B cells obtained from mice following the co-administration of unmethylated CpG oligonucleotides with the intraperitoneal administration of an allergen, comprising the SEA antigen. The specification fails to teach the successful treatment and prevention of any and/or all bacterial infections in an organism comprising the administration of CpG containing oligonucleotides. One skilled in the art would not accept on its face the examples given in the specification of the conversion from a Th2 to a Th1 immune response in B cells following the co-administration of unmethylated CpG containing oligonucleotides with an allergenic antigen in mice, or the conversion from a Th2 to a Th1 immune response in human B cells in vitro following the administration of unmethylated CpG containing oligonucleotides, as being correlative or representative of the prevention of any

and/or all bacterial infections in an organism in view of the lack of guidance in the specification and known unpredictability associated with the appropriate administration and successful in vivo delivery of such oligonucleotides in an organism whereby treatment effects and prevention are provided for any and/or all bacterial infections. The specification as filed fails to provide any particular guidance which resolves the known unpredictability in the art associated with the appropriate administration and in vivo delivery of CpG oligonucleotides in an organism, whereby bacterial infections are prevented in that organism.

The breadth of the claims and the quantity of experimentation required. The breadth of the claims is very broad. The claims are drawn to the treatment and prevention of any bacterial infection in an organism comprising the administration of CpG containing oligonucleotides. In order to practice the invention over the scope claimed, it would require undue trial and error and undue experimentation beyond which is taught in the specification, whereby the administration of any CpG containing oligonucleotide - by any route, and at any time, relative to the exposure of an organism to an infectious bacteria - provides for treatment effects and prevention of any bacterial infection. The quantity of experimentation required to practice the invention as claimed would require the de novo determination of appropriate modes of delivery, including appropriate formulations and the appropriate timing of the administration of the CpG containing oligonucleotides relative to the organism's exposure to an infectious bacterial agent, to target appropriate cells and /or tissues, whereby any bacterial infection is prevented in vivo, and that treatment effects are provided for any and/or all bacterial infections

in an organism. Since the specification fails to provide any particular guidance for the successful prevention of bacterial infections in an organism, and since determination of these factors is highly unpredictable, it would require undue experimentation to practice the invention over the scope claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 104 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 37 of U.S. Patent No. 6,239,116. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1 and 37 of USPN 6,239,116, which are drawn to methods of stimulating an immune response (comprising inducing Il-6 and Il-12) in a subject comprising administering an immunostimulatory, unmethylated CpG containing oligonucleotide to a subject, embrace the

claim of the instant application, which comprises a method of treating a bacterial infection (i.e. including inducing Il-6 and Il-12) in a subject, comprising the administration of a CpG containing oligoncucleotide.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ

March 26, 2002

1616

File

Application/Control Number: 09/630,319

Art Unit: 1635

The Paper No 8 filed on ***January 22, 2002*** (certificate of mailing dated ***January 14, 2002***) have not been made part of the permanent records of the United States Patent and Trademark Office (Office) for this application (37 CFR 1.52(a)) because of damage from the United States Postal Service irradiation process. The above-identified papers, however, were not so damaged as to preclude the USPTO from making a legible copy of such papers. Therefore, the Office has made a copy of these papers, substituted them for the originals in the file, and stamped that copy:

COPY OF PAPERS

ORIGINALLY FILED

If applicant wants to review the accuracy of the Office's copy of such papers, applicant may either inspect the application (37 CFR 1.14(d)) or may request a copy of the Office's records of such papers (*i.e.*, a copy of the copy made by the Office) from the Office of Public Records for the fee specified in 37 CFR 1.19(b)(4). Please do **not** call the Technology Center's Customer Service Center to inquiry about the completeness or accuracy of Office's copy of the above-identified papers, as the Technology Center's Customer Service Center will **not** be able to provide this service.

If applicant does not consider the Office's copy of such papers to be accurate, applicant must provide a copy of the above-identified papers (except for any U.S. or foreign patent documents submitted with the above-identified papers) with a statement that such copy is a complete and accurate copy of the originally submitted documents. If applicant provides such a copy of the above-identified papers and statement within **THREE MONTHS** of the mail date of this Office action, the Office will add the original mailroom date and use the copy provided by applicant as the permanent Office record of the above-identified papers in place of the copy made by the Office. Otherwise, the Office's copy will be used as the permanent Office record of the above-identified papers (*i.e.*, the Office will use the copy of the above-identified papers made by the Office for examination and all other purposes). This three-month period is not extendable.